CENTER FOR DRUG EVALUATION AND RESEARCH

Guidance for Industry

The FDA published Good Guidance Practices in February 1997. This guidance was developed and issued prior to that date.

Additional copies are available from:
Office of Training and Communications
Division of Communications Management
Drug Information Branch, HFD-210
5600 Fishers Lane
Rockville, MD 20857

(Tel) 301-827-4573
(Internet) http://www.fda.gov/cder/guidance/index.htm

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES, FOOD AND DRUG ADMINISTRATION

HEW(FDA) 78-3067

GUIDELINES FOR THE CLINICAL EVALUATION OF LAXATIVE DRUGS

April 1978

Comments on the contents of this publication are invited and should be addressed to the following office:

Director
Division of Cardio-Renal Drug Products
Bureau of Drugs
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

For sale by the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402

ABSTRACT

The Food and Drug Administration, with the assistance of its scientific Advisory Committees and other outside consultants, the American Academy of Pediatrics' Committee on Drugs, and consultants to the Pharmaceutical Manufacturers' Association has developed guidelines for the clinical evaluation of new drugs. These guidelines present acceptable current approaches to the study of investigational drugs in man, and pertain to Phases I through III of the investigation. They represent generally accepted principles for arriving at valid conclusions concerning safety and effectiveness of new drugs, as well as the views of outstanding experts concerning appropriate methods of study of specific classes of drugs.

The FDA welcomes comments on the guidelines, and expects to keep them current by review and update at approximately two-year intervals.

FOREWORD

The purpose of these guidelines is to present acceptable current approaches to the study of investigational drugs in man. These guidelines contain both generalities and specifics and were developed from experience with available drugs. It is anticipated that with the passage of time these guidelines will require revision. In order to keep them current a re-review will be performed approximately every 18 to 24 months.

These guidelines are not to be interpreted as mandatory requirements by the FDA to allow continuation of clinical trials with investigational drugs or to obtain approval of a new drug for marketing. These guidelines, in part, contain recommendations for clinical studies which are recognized as desirable approaches to be used in arriving at conclusions concerning safety and effectiveness of new drugs; and in the other part they consist of the views of outstanding experts in the field as to what constitutes appropriate methods of study of specific classes of drugs. In some cases other methods may be equally applicable or newer methods may be preferable, and for certain entirely new entities it is possible that the guidelines may be only minimally applicable.

Under FDA regulations (21 CFR 10.90(b)) all clinical guidelines constitute advisory opinions on an acceptable approach to meeting regulatory requirements, and research begun in good faith under such guidelines will be accepted by the Agency for review purposes unless this guideline (or the relevant portion of it) has been formally rescinded for valid health reasons. This does not imply that results obtained in studies conducted under these guidelines will necessarily result in the approval of an application or that the studies suggested will produce the total clinical information required for approval of a particular drug.

Many of the clinical guidelines have been developed largely, or entirely, by FDA's Advisory Committees and consultants. Others were originally developed by intramural committees and consultants of FDA and of the Pharmaceutical Manufacturers Association; in these cases the guidelines were reviewed and revised, as appropriate, by FDA's Advisory Committees.

The general guidelines for the evaluation of drugs in infants and children and most of those for study of various drug classes in children were developed by the Committee on Drugs of the American Academy of Pediatrics (AAP). Some of the pediatric guidelines for specific classes were written by FDA's Advisory Committees. There was cross review and comment on the pediatric guidelines by both the Committee on Drugs of the AAP and FDA's Advisory Committees.

The Bureau of Drugs of the FDA wishes to thank the many individuals who devoted so much time and effort to the development of these guidelines.

J. Richard Crout, M.D.
Director
Bureau of Drugs

Marion J. Finkel, M.D.
Associate Director for
New Drug Evaluation
Bureau of Drugs

GUIDELINES FOR THE CLINICAL EVALUATION OF LAXATIVE DRUGS

"General Considerations for the Clinical Evaluation of Drugs" is an important companion piece and should be reviewed prior to reading these guidelines. It contains suggestions which are applicable to investigational drug studies for most classes of drugs and enables elimination of repetitious material in each of the specific guidelines.

I. INTRODUCTION

A. Definitions

1. Laxative Agent--This is defined as any agent that promotes evacuation of feces from the lower bowel. As used herein, the term "laxative" denotes any agent that induces evacuation of any significant degree; it includes the terms "cathartic" and "purgative" (the difference among these terms is largely one of degree--cathartic and purgative agents cause more rapid evacuation responses with obvious alteration in stool consistency; actions of a laxative are assumed to be less pronounced but larger doses may produce a cathartic effect).

2. Constipation--Constipation is defined as infrequent (compared to the normal bowel evacuation range) and/or difficult and painful evacuation of hard feces.

3. Normal Bowel Movement Pattern--This may be defined in terms of frequency and consistency of spontaneously passed bowel movements. Fewer than three bowel movements per week or more than three bowel movements per day is considered abnormal. Also considered abnormal would be passage of three voluminous, watery, diarrheal stools per week or daily passage of inspissated, small movements accompanied by rectal discomfort. No simple correlation between bowel patterns and age has been demonstrated.

II. PHASE I STUDIES

A. **Variables Appropriate for Study**--Bowel movement patterns (changes in fecal contents, modification of mucosal function, and alteration in motor activity of the gastrointestinal tract) may be influenced by laxative agents. In Phase I studies, the following aspects of laxation might be considered for evaluation:

1. Frequency of bowel movements (number of spontaneous evacuations per unit time)

2. Description of bowel movement and appraisal of ease of passage

   a. Subjective

      (1) Consistency (liquid, soft, hard)

      (2) Shape (scybalous, pencil-shaped, etc.)

(3) Passage (painful, burning, tenesmus)

(4) Density (floating, etc.)

b. Objective--Rheologic or other physical characteristics

3. Volume (ml/unit time)

4. Weight (g/unit time)

5. Water content (% of water in aliquot)

6. Fecal solids (g/aliquot)

7. Bulk density (weight/unit volume)

8. Transit time ("time method" or "distance method" using various markers)

9. Fecal excretion rate (g/hr)

10. Other (stool content of electrolytes, bile acids, enzymes, etc.)

It is not necessary to measure all of the variables outlined above in all subjects studied in Phase I; however, it is imperative that the appropriate mechanisms be evaluated in a sufficient number of subjects to provide meaningful data.

Examples of specific objective measurements that could be made to document specific claims include:

1. Inhibition of enzyme activity (Na+, K+ - ATPase--e.g., by bisacodyl, phenolphthalein, dioctyl sodium sulfosuccinate (DSS))

2. Increase in cyclic AMP (castor oil, bile acids)

3. Osmotic attraction (salt solution, glycerin, sorbitol, cellulose)

4. Stimulation of reflex action (myoelectrical studies--bisacodyl)

5. Rheologic studies (stool-softeners, lubricants, detergents)

6. Transit time studies (bulk-formers)

7. Distention (bulk-formers, fiber, carbon dioxide-releasing agents)

8. Other (formation of volatile fatty acids; perfusion studies; specific radiologic studies)

A claim that the test drug promotes bowel evacuation must be documented by studies using appropriate techniques. For example, if laxative action is claimed due to inhibition of nonspecific Na+, K+-ATPase or cyclic AMP, this fact should be documented by assay for enzymatic activity.

B. Classes of Laxative Agents--There are a number of effective and safe laxative agents that may be classified in the following categories, among others:

1. Bulk-formers (absorbents)

2. Stimulant laxatives (secretory and/or motor activity)

3. Saline laxatives

4. Hyperosmotic agents

5. Lubricants

6. Stool softeners

7. Miscellaneous (e.g., carbon dioxide-releasing agent, bile acids)

C. **Procedures for Documenting Mechanism of Action of Symptom Relief**--If a specific mechanism of action is proposed for the laxative agent, the mechanism should be clearly stated and documented by appropriate procedures. If no mechanism of action is proposed, this fact should be clearly stated and the symptoms from which relief is claimed to be achieved by the drug should be documented by appropriate means. It is recognized that the mechanism of action of many safe and effective drugs is unknown. Nonetheless, presentation of data to elucidate the pharmacologic effects of laxative agents is encouraged.

D. **Drug Effects Other Than the Specific Effects Under Study**--In addition to promoting bowel evacuations, the test agent may have other important systemic action such as effects on gastrointestinal secretions, sphincter tone and function, propulsive motor activities, the central nervous system, the cardiovascular system, release of gastrointestinal hormones, release of prostaglandins, acid-base balance, or serum electrolyte values. When the bowel lumen is narrowed, bulk-forming agents might precipitate intestinal obstruction.

E. **Adverse Effects**--Provision should be made for reporting, and, if appropriate, measuring all adverse effects. To avoid difficulties in interpreting side-effects, subjects should be excluded from Phase I studies if they have a significant history of allergy. There are specific adverse effects that should be looked for with certain classes of laxative agents--for example, nausea and vomiting, impaired absorption of essential nutrients, severe abdominal cramping, or electrolyte depletion. If the test drug is a bulk-former to be taken orally, particular attention should be given to the possibility of obstruction in the esophagus, small bowel, or colon as a result of an unsuspected stricture or narrowing of the lumen. Periodic reexamination of subjects should be performed at intervals appropriate for the drug under study.

F. Subjects

1. Subjects Appropriate for Study--Women with childbearing potential (including nursing mothers) shall be excluded. The number of subjects studied should be adequate to provide answers valid at reasonable statistical confidence levels to the specific questions being asked. Normal, healthy, adult males would be appropriate subjects. Protocols should indicate the sources from which the subjects are drawn.

2. Exclusions

   a. History of chronic gastrointestinal disease even though the subject is asymptomatic when being considered for the study

   b. Acute gastrointestinal disorder within the past 30 days

   c. Concomitant disease or therapy

3. Description of Study Population--Accurate description of the sample studied is needed. All subjects screened by the investigator for inclusion in the study and not accepted should be recorded with the reasons for rejection. Characteristics

of the study population with respect to age, sex, health status, and any other relevant variables should be recorded. The number of subjects included in the Phase I study should be restricted to that necessary for obtaining the required data.

G. Pretreatment Procedures

In addition to the usual "safety" laboratory studies, laboratory studies appropriate for the drug under study and pretreatment physical examination, the following should be performed and described:

1. Fasting of subjects and other necessary preparations should be specified.

2. Pattern of Bowel Movement--Appropriate methods of recording and documenting bowel movement patterns should be selected (see II A). This will depend on the aspects of laxation under study. The technique(s) selected should be used uniformly in all subjects and for a sufficiently long period to ensure obtaining meaningful data. A pretreatment workup should be performed in close proximity to the initiation of the drug study.

H. Treatment Period

1. Medication--All drugs utilized in the study should be described and the description should include dosage, dosage forms, and other relevant data for identification.

2. Dosage--The amount per dose and the number of doses of all drugs administered should be recorded.

3. Administration--The method of administration (routes) and the frequency of administration should be recorded.

4. Dose-Response--Once the safety level in single-dose studies is established, a dose-response curve may be constructed for incremental doses with sequential stepwise increases in dosage or other appropriate experimental design taking cognizance of the problem of fade.

5. Test Conditions--The variability in gastrointestinal motor and secretory activities and its influence on bowel movement patterns is incompletely known. Thus, it may be difficult to demonstrate and quantitate alterations in these activities. The relationship of gastrointestinal motor and secretory activities, especially in the colon, to bowel movement patterns has not been precisely defined, and many of the methods used to assess such relationships are imprecise. These methods include radiologic, tracer, perfusion, myoelectric, and biopsy techniques. The limitations of these methods must be recognized. The most appropriate method for documenting the claimed mechanism of action of the test drug should be used.

6. Observations During Treatment

The onset of action, the pharmacologic action, and the duration of action of the drug should be recorded.

a. Pharmacologic Action

(1) The claimed pharmacologic action should be documented by an appropriate technique.

(2) Data (preferably quantitative) on pharmacologic action should be in a form that can be subjected to statistical analysis.

(3) It is unacceptable to extrapolate or extend the claimof pharmacologic action beyond that demonstrated.

b. Serum Level of Drug--If the laxative agent is absorbed, one may wish to consider studies during Phase I or Phase II which would attempt to correlate, if possible, specific blood levels with specific changes in bowel movement patterns or relief of symptoms.

III. PHASE II STUDIES

A. Purpose

The purpose of these studies is to determine whether alteration in the bowel movement pattern or relief of symptoms or both differ in patients treated with the test drug and those treated with placebo or another reference drug in one or more of the following conditions:

1. Idiopathic constipation
2. Constipation secondary to change in routine (e.g., travel)
3. Constipation secondary to change in diet (decreased fiber content of diet in edentulous patients)
4. Constipation secondary to change in fluid intake (dehydration)
5. Constipation secondary to enforced bed rest
6. Irritable bowel syndrome (motility disorder)
7. Chronic constipation or obstipation (neuropathy, depression)
8. Bowel preparation for radiologic or endoscopic studies
9. Behavioral disorder characterized by stool retention
10. Postoperative convalescence
11. Constipation secondary to partial obstruction (inoperable surgical condition, late pregnancy)
12. Constipation secondary to specific or nonspecific drugs (narcotics, others)
13. Constipation secondary to anal disease (hemorrhoids, fissures, fistulas)
14. Other, to be specified

B. General Statements

1. Definition of Clinical Conditions--All of the above clinically-encountered conditions listed in these guidelines must meet certain diagnostic criteria to be included in Phase II studies. The bowel movement pattern must be such that fewer than three spontaneous bowel evacuations occur per week or bowel movements are more frequent but are of such inspissated consistency as to be painful. Patients in whom the bowel movement pattern is abnormal due to

rectal disease (hemorrhoids, fissures, fistulas, proctitis, etc.) can be included but should be stratified appropriately regarding clinical condition as well as the need for surgical intervention or other treatment. It must be determined with certainty that constipation of short duration is due to one of the causes listed above and is not due to serious organic disease (carcinoma of the colon, severe diverticular disease, proctitis, intestinal obstruction, inflammatory bowel disease, etc.). Admission to the clinical trial must be restricted to patients in whom the diagnosis is established by appropriate clinical criteria.

2. Evidence of Effectiveness

   a. Demonstration of modification of bowel movement pattern--These variables could include frequency, consistency, shape, ease of passage, volume, weight, water content, fecal solids, bulk density, transit time, fecal excretion rate, fecal content of electrolytes or bile acids, enzyme studies, or endoscopic evaluation.

   b. Relief of Symptoms--Partial or complete relief of previously defined specific symptoms.

   c. Improvement in Other Indices--Improvement in acceptable predefined specific indices (abdominal girth measurement, days lost from work, time of return to usual life style, morbidity, etc.).

C. Patients

Patients with bowel evacuation patterns ouside the normal range, who pass stool of abnormal consistency or with undue subjective discomfort, or who do not pass bowel movements spontaneously and who meet the diagnostic criteria outlined previously are appropriate for inclusion in the clinical trial. Thus, the clinical studies will be done in specific target populations.

The protocol should indicate the sources from which the patients are drawn. Each patient should meet the diagnostic criteria described in III.B.1. If more than one of these conditions exists, the protocol and data analyses should be designed appropriately. If pain is to be evaluated, there should be a definite diagnosis for the clinical condition and definite pain should be present for at least 2 of the 3 days preceding the test.

Patients are to be excluded under any of the following conditions:

1. Occurrence, within 30 days before the initiation of the drug trial, of complications that provide a compelling indication for surgical operation

2. More than one of the clinical conditions under consideration unless such patients are equally distributed in drug and placebo groups

3. Concomitant disease or therapy contraindicating trial with the test drug

4. Chronic alcoholics, drug abusers, or other persons whose reliability and physical status prevent proper evaluation of a drug trial, unless this is the target population to which the therapy is directed

Accurate description of the sample studied is needed. All subjects screened by the investigator for inclusion in the study and not accepted should be recorded with the reason for rejection. Characteristics of the study population with respect to age, sex, health status, and any other relevant variables should be recorded.

D. Pretreatment Procedures

In addition to the usual physical examination and laboratory studies appropriate to the drug under investigation, the pretreatment workup should include procedures necessary to establish or confirm the diagnosis. It should be performed in close proximity to the initiation of the drug study.

1. Bowel Movement Studies--Studies of bowel movement patterns and stool composition should be of sufficient duration to provide meaningful data and should be appropriate to the mechanism of action or the symptoms to be relieved.

2. Endoscopy should be performed by an experienced endoscopist (not a person in training). It is highly desirable that the same endoscopist do all of the endoscopic procedures on the same patient. Objectivity will be enhanced if a second observer records his findings independently at the same examination or if findings are documented photographically.

3. Radiologic examinations should be appropriate for the type of motility or drug effect under study and performed by an experienced radiologist. It is advisable for the same radiologist to do all the radiologic procedures on the same patient.

4. Gastrointestinal Motor and Secretory Activities--The procedures used should be appropriate for detecting and measuring changes in the activity under study.

5. Other Special Procedures--As indicated by the chemical composition of the test drug and the clinical condition under study. Special cognizance should be taken of the significant role dietary factors may play in bowel movement pattern; a daily dietary diary should be considered in these studies.

E. Study Design

The randomized plan should provide for stratification or a separate protocol according to the types of clinical conditions being investigated with specific groupings of symptoms to be treated. The following should be observed:

1. The target symptoms, laboratory indices, and other special procedures to be studied should be clearly specified.

2. A double-blind stratified and randomized design of drug studied in parallel against a placebo is most desirable. A reference drug of proven efficacy may be appropriately used in some studies.

3. Excluded patients should be accounted for.

4. Dropouts and discontinued patients should be followed up and reported.

5. Other treatments should be applied as uniformly as possible.

6. The crossover study design could be used when appropriate.

7. Appropriate statistical analyses of results as related to the originally stated target symptoms and other observations should be performed.

F. Treatment Period

1. Duration of Trial--The duration of the treatment period should be related to the objectives of the protocol.

2. Medication--Treatment is begun on the day after completion of the workup. Subjects are randomly assigned to the study groups. The method of random assignment should be specified in detail.

   a. Dosage

      (1) Dose schedule should be established before the study starts, and changes in dosage during the clinical trial should be avoided except when untoward effects occur.

      (2) Alternatively, different fixed dose levels may be assigned in the treatment group(s). Variation or adjustment of dosage for individual patients on the basis of symptom response alone is not encouraged.

   b. The placebo should be indistinguishable in form from the test drug and administered on the same predetermined schedule.

   c. If a reference drug is used, this also should be indistinguishable in form from the test drug and administered on the same predetermined schedule.

   d. Other Drugs--Patients should be advised not to take analgesics, antacids, sedatives, stimulants, salicylates, or tranquilizers. Since the patients probably will not follow this advice completely, the agents and amounts used should be recorded. Failure to follow this advice is not grounds for exclusion from the study. When other drugs must be prescribed, the specific drugs and the amounts used should be documented.

3. Diet--No specific diet need be imposed apart from avoidance of foods that tend to exacerbate the symptoms. A daily diet diary is recommended.

4. Setting--Patients included in the study should be in one of the following categories:

   a. Hospitalized

   b. Outpatient

   c. Fixed ratio, such as 1 week or less in the hospital and 2 weeks or more as an outpatient

5. Observations During Treatment

   a. Toxicity--Evaluation of the toxicity of the drug under study should be carried out with appropriate observations and laboratory tests performed at specified intervals. Mechanisms for early detection of toxicity as manifested by signs, symptoms, or laboratory evidence must be built into the protocol. Specific procedures for withdrawal of the patient from the study because of toxicity should be stated in the protocol.

   b. Withdrawal of patients from trial by physician

      (1) Withdrawals will be made for reasons of toxicity or when deemed clinically appropriate because of changes in severity of illness or development of complications.

      (2) There should be preestablished criteria for withdrawals.

      (3) The reason for withdrawals should be concisely identified.

(4) Patients withdrawn from the study should be followed until the resolution of the condition requiring the withdrawal.

(5) Results should be analyzed in three groups: (a) all who started on study including those who withdrew, (b) only those who completed study, and (c) only those who withdrew from study.

c. Indices of effectiveness--The observations required for those indices of effectiveness that have been selected for study should be carried out at specified intervals and recorded systematically during the study. These indices include but are not restricted to those enumerated in II A, above. Selected procedures and laboratory determinations may have to be repeated several times during the treatment period in order to detect cumulative effects or the development of tolerance.

Daily diary or evaluation sheets should be kept by the patient during the treatment period.

There should be uniform periodic visits to the physician with recorded evaluations (rating scales, etc.) until a predetermined end point has been reached.

G. Observations After Treatment

Appropriate followup observations should be made in order that possible delayed adverse effects are not overlooked.

H. Data Analysis

Appropriate statistical analyses of results as related to the originally stated target symptoms, laboratory tests, and special procedures should be done.

The protocol should state in advance what will be considered evidence of effectiveness, keeping in mind that statistical significance is not necessarily clinical significance. All data pertaining to indices of efficacy should be recorded on forms designed for that purpose and specified in the protocol. Diaries, symptom-rating scales, and physician and patient assessment forms should be used as appropriate. These should be pretested and shown to be workable before the study is begun.

The method of scoring each index of effectiveness should be clearly defined in the protocol. The method(s) of statistical analysis of the scores of each index of effectiveness should be clearly stated in the protocol, with literature references. (An acceptable model for a grading scale would be: 0 = none; 1 = present but patient able to carry on usual activities; 2 = interferes with usual activities; 3 = disabling.) Keeping the number of grades as few as possible facilitates the assessment. There may be certain circumstances in which grading may include some stratification. The increments of grades should be as nearly equal as possible. When possible, statistical and clinical significance should be correlated.

Analysis of results should be carried out in such a way as to first include and then exclude withdrawals; results for withdrawals alone also should be analyzed. Withdrawals include patients who withdraw from the study on their own as well as patients dropped from the study by the investigator for failure to comply with the protocol (defined here as failure to take the test drug). Reasons for withdrawal of the patient by the investigator should be recorded. Patients who do take the drug but use other medications or substances or diets that are not prescribed by the protocol should be grouped separately and included.

III. Effectiveness Standards

Clinical studies should be done in specific populations that meet specific diagnostic criteria. Appropriate stratification within each specific diagnostic category should be carried out at the time of data analysis to delineate efficacy of the test drug in the setting of varying degrees of severity of the disorder. In some instances, it may be advisable to stratify patients as to age, sex, and duration of disease before randomization. In addition to data obtained pretreatment and during treatment any preexisting conditions that might bias analysis should be taken into consideration in the analysis of the data. Efficacy can also be shown by comparison of effects of a placebo or reference drug with those of the drug to be tested in the same patient as well as between groups of patients. Although a study design in which a patient serves as his own control may sometimes be used to demonstrate effectiveness of a new agent, if such a design is used it is essential to allow an adequate interval between drug and placebo treatment periods so that all indices under study may return to baseline levels. The duration of this interval will be determined by the compound being tested, the clinical condition being treated, and the indices under evaluation.

In general, the criteria to be met for a new agent to be classified as an effective laxative drug must include: (1) the demonstration by appropriate methods that the drug promotes bowel movement; and (2) the demonstration that the drug effects improvement in predefined symptoms indices.

IV. PHASE III STUDIES

This represents an extension of Phase II to include patients treated for longer periods (as determined by the natural course of the clinical entity and patterns of recurrence) to evaluate increased risks, to detect complications, and to explore safety and effectiveness under conditions of clinical practice. In this Phase, it is not necessary to demonstrate modification of bowel evacuation pattern in patients with specific clinical entities. Appropriate indices of clinical evaluation, including physical examinations and laboratory tests, should be monitored to detect evidence of toxicity. To demonstrate additional significant evidence of effectiveness, appropriate clinical studies should be designed and performed.

The ABSTRACT CARDS below are designed to facilitate document retrieval using Coordinate Indexing. They provide space for an accession number (to be filled in by the user), suggested keywords, bibliographic information and an abstract.

The Coordinate Index concept of reference material filing is readily adaptable to a variety of filing systems. Coordinate Indexing is described in the publication "IBM Data Processing Techniques - Index Organization for Information Retrieval" (C 20 8062). Copies are available through IBM Branch Offices.

The cards are furnished in triplicate to allow for flexibility in their use (for example, author card index, accession number card index).

GUIDELINES for the CLINICAL EVALUATION of ANTACID DRUGS.
U.S. Department of Health, Education, and Welfare, PHS, Food and Drug Administration, Bureau of Drugs. HEW Publication (FDA) 78-3065, GPO 017-012-00261-7 (April 1978) 10 pp.
Accession No.
ABSTRACT: Guidelines developed by FDA assisted by its scientific Advisory Committees, and consultants from industry and academia. Represent acceptable current approaches to the study of investigational drugs in man for Phases I through III of the investigation; embody general principles required to permit valid conclusions concerning safety and effectiveness of
(Over)

GUIDELINES for the CLINICAL EVALUATION of ANTACID DRUGS.
U.S. Department of Health, Education, and Welfare, PHS, Food and Drug Administration, Bureau of Drugs. HEW Publication (FDA) 78-3065, GPO 017-012-00261-7 (April 1978) 10 pp.
Accession No.
ABSTRACT: Guidelines developed by FDA assisted by its scientific Advisory Committees, and consultants from industry and academia. Represent acceptable current approaches to the study of investigational drugs in man for Phases I through III of the investigation; embody general principles required to permit valid conclusions concerning safety and effectiveness of
(Over)

GUIDELINES for the CLINICAL EVALUATION of ANTACID DRUGS.
U.S. Department of Health, Education, and Welfare, PHS, Food and Drug Administration, Bureau of Drugs. HEW Publication (FDA) 78-3065, GPO 017-012-00261-7 (April 1978) 10 pp.
Accession No.
ABSTRACT: Guidelines developed by FDA assisted by its scientific Advisory Committees, and consultants from industry and academia. Represent acceptable current approaches to the study of investigational drugs in man for Phases I through III of the investigation; embody general principles required to permit valid conclusions concerning safety and effectiveness of
(Over)

new drugs; also the views of outstanding experts concerning appropriate methods of study of antacid drugs.
FDA welcomes comments on the guidelines, and expects to keep them current by review and update at approximately two year intervals.
KEYWORDS: Clinical guidelines; drug testing; Phases I-III; antacid drugs.

new drugs; also the views of outstanding experts concerning appropriate methods of study of antacid drugs.
FDA welcomes comments on the guidelines, and expects to keep them current by review and update at approximately two year intervals.
KEYWORDS: Clinical guidelines; drug testing; Phases I-III; antacid drugs.

new drugs; also the views of outstanding experts concerning appropriate methods of study of antacid drugs.
FDA welcomes comments on the guidelines, and expects to keep them current by review and update at approximately two year intervals.
KEYWORDS: Clinical guidelines; drug testing; Phases I-III; antacid drugs.